

RARE TUBERCLE BACILLI IN SPUTUM: THEIR SIGNIFICANCE*

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IN a previous paper the authors discussed the difficulty of rendering sputum negative when once positive for tubercle bacilli. We showed in detail the after-history of a group of patients who were followed for as many as fifteen years and reexamined at intervals after treatment had ceased, and stated that it was our opinion that "completely and permanently negative sputum is rarely attained in those who have suffered from destructive and especially widespread pulmonary tuberculosis, even though they are clinically well and able to do their usual work."

Some workers have misunderstood our statement, thinking that we are of the opinion that tuberculous patients, when once showing bacilli in the sputum, rarely become free. On the contrary, of the eleven cases reported in our study, two, who were suffering from a recent exudative invasion (one with, the other without cavity) were both bacillus-free on all subsequent sputum examinations; and a third, who had an acute bilateral infiltration with cavitation in both lungs, became free, and rare bacilli were found on two occasions only, two and four years after the end of treatment.

DIFFICULTY IN RENDERING SPUTUM NEGATIVE

Our opinion of the difficulty in rendering sputum negative is based on our own experience with a refined technique, by which bacilli may be found when an entire specimen examined, even though it be saved for seventy-two hours, may not contain more than a few hundred bacilli. This technique gives 20 to 250 times (average 80 times) as many bacilli in a unit time of search as the Ziehl-Neelsen method. The average is made from over 400 comparisons. The technique is relatively more efficient in the examination of purulent specimens than in those muco-epithelial in character.

Our patients consist of all cases who have come under our care in the past twenty years, both in the sanatorium and in the clinic; and inasmuch as we give our services to all who desire them, the prognosis of many of our patients is unfavorable when first seen. Some even are beyond the possibility of improvement, let alone healing. We also have a large group with minimal lesions, or who have previously recovered from limited lesions, most of whom are negative at the time of examination. Many of these are clinic cases.

SPECIMENS FROM 3,794 PATIENTS

At this time we are discussing 3,794 patients

on whom 27,405 examinations were made. Of this number 2,847 (75.1 per cent) were always positive, and 947 (24.9 per cent) were intermittently positive and negative.

Our advanced cases were usually suffering from extensive disease, and bilaterally involved. Our patients were treated by all of the usual methods, physiological and surgical, always giving the physiological methods a chance before using compression. It is our experience that those cases which produce the best results under compression are the ones which do the best without it. Furthermore, by waiting we find that many which seemed to call for pneumothorax are able to heal spontaneously. In our experience, we have found that patients whom we consider suitable for hygienic treatment, pneumothorax or thoracoplasty, all respond to treatment with rare and negative sputum to about the same degree. Only thirty per cent of our patients give negative guinea-pig tests, with a 15-day inoculum, after showing three successive negative tests by dilution-flotation. Some of these who still show rare bacilli when they leave the institution will become negative with the passing of time, as we have found by our follow-up examinations.

Of 947 patients who were intermittently positive and negative, bacilli were found on 5,837 examinations, and were absent 4,436 times. Of 365 patients in whom tubercle bacilli were reported positive by dilution-flotation, all would probably have been negative by Ziehl-Neelsen. Some 243 of these were confirmed by guinea-pig; 30 more were examined once only, but had carried bacilli in abundance on previous occasions; and 92 patients of the group were examined but once, without confirmation by guinea-pig test.

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DISAPPEARANCE OF TUBERCLE BACILLI FROM PULMONARY EXCRETIONS FOLLOWING TREATMENT*

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WE are well aware of the chronicity of tuberculosis and its tendency to relapse. We could readily find plenty of cases to demonstrate the persistence of positive sputum following treatment, but the object here is to show the optimistic side.

SPUTUM EXAMINATION PROGRAM

Our sputum examination program includes at least one test in each calendar month. The procedures employed are direct smear, flotation-concentration, culture, animal inoculation, and stomach contents examinations. In our flotation-concentration test, the smears are examined each period of 10 minutes. For culture, the sputum is dissolved in $\frac{1}{2}$ per cent sodium hydroxide,

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* From the Barlow Sanatorium, Los Angeles.
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treated with oxalic acid 2½ per cent, centrifuged, and the sediment planted on two tubes of Petrag-nani's medium. For animal tests the sputum is shaken with ½ per cent sodium hydroxide, centrifuged, the sediment washed and then inoculated subcutaneously into a guinea pig. The animals are allowed to go two months before autopsy if clinically negative. Visceral disease is required as evidence of tuberculosis. Stomach contents are examined only by culture and animal inoculation.

All direct smears are on 24-hour specimens. Concentrations, cultures and animal inoculations were on three-day specimens up to February, 1939, and thereafter on six-day specimens unless the patient expectorated unusual quantities of sputum. The six-day specimens are collected two days at a time and ice-boxed until the whole amount can be pooled and examined. Concentration has always been accompanied by culture done simultaneously on the same specimen. Culture is now frequently done alone, but concentration never without culture. During the past four and one-half years culture and inoculation of a six-day sputum specimen have been carried out at the same time as culture and inoculation of the stomach contents.

As a rule, the simplest test that will demonstrate the bacilli is used. When the patient becomes negative to one procedure the next more sensitive test is used. When negative to concentration and culture, or to culture alone, for three months, gastric lavage is performed with culture and inoculation of both sputum and stomach contents. In patients remaining negative, gastrics are performed about every 4th month.

THIRTY-DAY SPUTUM TESTS

A number of years ago the question arose as to whether we were really getting our patients negative. It was suggested that, if we inoculated all the sputum expectorated for one month into a guinea pig, most of our presumed "negative" patients would be shown to be "positive." Therefore, in June, 1938, we began performing 30-day sputum inoculations on those patients negative to all tests for six or more months. This means they will have been negative to at least one gastric examination. The sputum is collected two days at a time and ice-boxed. When a six-day batch has been accumulated, it is treated and inoculated. Inoculations are made in the right and left inguinal region and, if necessary, in the right and left axillary regions. Sometimes only one guinea pig was used, sometimes four, but usually two. Beginning in June, 1939, simultaneous concentration and culture were performed along with animal inoculation, but the specimens were not divided until they had been thoroughly dissolved and broken up by shaking with sodium hydroxide.

From June, 1938 to January, 1944, one or more 30-day tests have been performed on each of 86 patients. Of these 72 or 83.7 per cent were negative to animal inoculation as well as to concentration and culture.

Of the 14 patients that were positive ten were positive by animal alone, two by culture and animal, one by culture alone and one by concentration alone.

BACILLARY RECORDS OF PATIENTS DISCHARGED IN THE PAST SIX YEARS

A group of 284 patients who were resident in the Sanatorium six months or more, and who were positive at some time during their stay were studied. The disease rating is minimal in 18.3 per cent, moderately advanced in 50.5 per cent and far advanced in 31.2 per cent. Straight bed rest was the only treatment in 66 or 23.3 per cent, while lung collapse of one variety or another was applied in 218 or 76.7 per cent. The collapse therapy group is divided as follows pneumothorax alone or combined in 60 per cent, thoracoplasty as the principal treatment in 3.9 per cent, phrenic paralysis alone in 11.5 per cent, and other procedures in 1.3 per cent.

First, the group of 284 discharges was classified according to the number of months their sputum and gastric tests were negative prior to discharge and it was found that 46.1 per cent of all the patients in this group had "negative" tests four or more months prior to discharge, including at least one stomach contents examination. Twenty-eight per cent of them were negative eight months or more, including at least two "gastrics" and a 30-day sputum test in most cases.

TOTAL DAYS OF SPUTUM NEGATIVE PRIOR TO DISCHARGE

Next, it is of interest to record the total number of days of total sputum output examined and found negative by culture, concentration and culture, or inoculation prior to discharge, the intervening "gastrics" being negative, and this showed 116 patients or 40.8 per cent had 19 or more days of negative sputum and 91 patients, or 32 per cent, had 31 or more days of negative sputum prior to discharge.

FOLLOW-UP EXAMINATIONS

For several years we have attempted (when the technical help was available) to carry out a systematic follow-up examination schedule on ex-patients.

Recently, we have tried to perform gastric lavage, plus culture and inoculation, of a three-day sputum specimen in all cases except those known to be strongly positive, and here only sputum examinations have been done. The data below is for culture, flotation and culture or better.

One or more tests were performed on each of 236 expatients.

The examinations cover postsanatorium periods of from 3 months to 6 years, as follows:

- 3 months, 6 months and 1 year, in 78 cases;
- 2 to 3 years, inclusive, in 103 cases;
- 4 to 6 years, inclusive, in 55 cases.

The number of individual tests for each patient varied from 1 to 19, as follows:

- 1 to 2 tests, inclusive, in 101 cases;
- 3 to 4 tests, inclusive, in 88 cases;
- 5 to 6 tests, inclusive, in 30 cases; and
- 7 to 19 tests, inclusive, in 17 cases.

In 146 cases, or 61.9 per cent, all the tests were negative. In each of 90 cases, at least one test was "positive."

FOLLOW-UP RESULTS ACCORDING TO DISCHARGE RESULTS

It is of considerable importance to know the prognostic significance of negative sputum and stomach contents persistently and continuously present as a result of treatment. We do not feel that our follow-up examinations have been carried out for a long enough time by the more sensitive methods to adequately evaluate this point. However, the material at hand is suggestive. Below, follow-up results are classified according to the number of months the patient was negative prior to discharge:

- 0 to 1 month, follow-up tests negative in 41.3 per cent;
- 2 to 3 months, follow-up tests negative in 56.3 per cent;
- 4 to 7 months, follow-up tests negative in 76.1 per cent;
- 8 to 11 months, follow-up tests negative in 78.4 per cent; and
- 12 months or more, follow-up tests negative in 83.9 per cent.

These data indicate that the longer a patient is completely negative as the result of treatment, the more likely he is to remain "negative" in later years.

REPORT OF CASE

A young woman with moderately-advanced tuberculosis was given artificial pneumothorax which was improved by intrapleural pneumonolysis. Because of unusual circumstances, she was resident in the Sanatorium throughout her treatment. She became abacillary after nine months, and remained so for 54 months before and for one year after discharge. This represents a total of 272 days of "negative" sputum. It includes 28 concentrations and cultures, 21 cultures alone, two 30-day tests (one by guinea pig alone and one by concentration, culture and guinea pig), 13 gastric examinations by culture and guinea pig inoculation, and nine sputum inoculations with the gastrics and one alone. There were 17 negative tests after the lung had expanded, including six gastrics and six sputum inoculations covering a period of two years. (Editor's Note: Other case histories have been omitted to conserve space.)

COMMENT

In spite of persistent examination, including the most sensitive tests available, the tubercle bacilli disappear from the pulmonary excretions of almost half our patients following treatment. The sputum and stomach contents remain abacillary during at least 4 months of residence and, in the great majority, throughout the follow-up period of from three months to six years. Forty

per cent of those whose sputum is not converted while resident in the sanatorium become "negative" later on. Nearly one-third of pneumothorax cases studied had had lungs expanded.

The absence of tubercle bacilli from the pulmonary excretions does not necessarily mean there is no active disease in the lungs. The lesion may be healed or it may be just closed off. The closed lesion, of course, may open again, and this happens fairly often.

On the other hand, the continued output of virulent microorganisms is a constant danger to the patient, to his family and associates, and to the general public.

It is true this situation is, in many cases, consistent with health and long life. But probably, in many more instances, the disease reactivates and spreads to other parts of the lungs, requiring further institutional treatment or resulting in death.

Even more important is the public health hazard of the bacillus-distributing person. Perhaps the ultimate solution of the tuberculosis problem will require elimination of such sources of infection.

Although the permanent disappearance of tubercle bacilli from the pulmonary excretions of all cases is our ideal, it has not been attainable. We are faced with the necessity of discharging still "positive" patients, although the majority are expectorating relatively few bacilli, detectable only by the more sensitive tests. The best we can do for these people is to teach them a way of life consistent with health, and to teach and impress upon them a few simple rules of hygiene which, if followed, will largely prevent infection in others.

SUMMARY

1. Patients negative for six months or more to an intensive sputum examination program were tested by animal inoculation of all the sputum expectorated for one month. These tests were completely negative in 83.7 per cent.

2. Of the patients discharged from the Sanatorium between 1937 and 1943, 284 were here six months or more. Of these 46.1 per cent became negative as the result of treatment, and remained so four or more months prior to discharge, and 28.0 per cent eight or more months.

3. In the same group 40.8 per cent had 19 or more days of negative sputum; 32.0 per cent, 31 or more days.

4. Follow-up examinations were performed in 236 out of 284 cases. From one to 19 or more tests were done over a period of three months to six years. In 61.9 per cent all of the tests were negative.

5. The percentage of negative follow-up tests is directly proportional to the number of negative months prior to discharge, varying from 41.3 per cent in those not converted, to 83.9 per cent in those negative 12 months or more before leaving the Sanatorium.

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